Electroconvulsive Therapy in Depression

Current Practice and Future Direction

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KEYWORDS

• Electroconvulsive therapy • Neuromodulation • Treatment-resistant depression • Major depression • Review • Electrode placement • Cognitive side effects

KEY POINTS

- Electroconvulsive therapy (ECT) in conjunction with pharmacotherapy is superior to pharmacotherapy alone for management of treatment-resistant depression.
- Psychotic features and increased age are both positive predictive factors for a response to ECT. Acknowledging positive predictive factors can assist providers in deciding whether a patient would be a good candidate for ECT.
- Flexible treatment schedules after the acute course could improve remission rates and reduce unnecessary side effects.
- ECT tolerability and cognitive side effects can be improved by individualizing ECT treatment parameters.
- With refinements in the ECT technique for the treatment of special populations suffering from depression, complex medical conditions can be treated safely with ECT with fewer medical complications.

INTRODUCTION

It has been estimated that within the next 20 years depression will be the leading cause of disability in high-income nations.[1] Although pharmacotherapy may be effective for many with major depressive disorders (MDD), one-third of individuals will not

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respond to antidepressants.[2] As a result, a significant group of individuals with MDD will require alternative therapeutic modalities to address their depression. ECT has robust evidence to support its use in the treatment of MDD, particularly in patients with severe presentation of illness.

Unfortunately, electroconvulsive therapy (ECT) has historically suffered a damaging stigma that has limited its use. Much of the negative opinion can be traced back to the early years of ECT when it was administered without muscle relaxants and anesthesia. Memory loss remains a common primary concern among patients with ECT; however, the ECT electrode placement and parameters can now be modified to decrease the risk for that potential side effect. In addition, ECT machines used before the mid 1980s relied on a sinusoidal pulse wave that has been linked to significant cognitive deficits compared with the ultrabrief (UB) and brief (B) pulse waves that are used with modern technology.[3]

This article is intended to provide psychiatrists with a balanced, in-depth look at the recent advances in ECT technique as well as the evidence of ECT for managing depression including MDD in patients with comorbid medical problems.

THE MECHANISM OF ACTION

The mechanism of action of ECT remains poorly understood. Hypotheses range from ECT's involvement in targeting neurotransmitter and neuroendocrine dysregulation, GABAergic anticonvulsant effects, and involvement on the molecular level. Because ECT triggers a generalized seizure, there are biological changes that cannot be attributed to a singular mechanism of action.

ECT treatments are associated with normalization of hypothalamic–pituitary–adrenal axis in depressed patients, supporting a neuroendocrine mechanism.[4] The anticonvulsant theory,[5] the most widely accepted hypothesis, is based on the observation that ECT treatments result in an increase in the seizure threshold and a decrease in seizure duration over a course of ECT treatments. gamma-Aminobutyric acid (GABA) has been postulated as a key mediator of the ECT anticonvulsant effect.[5] The changes in GABA transmission secondary to ECT suggest that there may be an increase in tonic inhibition after repeated seizures.[6] The glutamate system is intrinsically related to GABA.[7] Seizures are accompanied by acute release of glutamate, which serves as the predominant mode of excitatory neurotransmission in the brain,[8] possibly causing the cognitive side effects.[9]

Imoto and colleagues[10] demonstrated that inducing seizures in animal models profoundly changed biochemical and physiologic features of mature granule cells in the hippocampal dentate gyrus (DG), more so than selective serotonin reuptake inhibitors treatments. The investigators of the same study suggested that "dematuration" of neurons in the DG could be a common cellular basis for antidepressant therapy.

Narp, an immediate early gene induced by electroconvulsive seizures (ECS), plays a key role in brain-derived neurotrophic factor (BDNF)–dependent synaptic modulation.[11] With repeated ECS, a rise in Narp protein can persist for nearly 24 hours, agglomerating in the hippocampus.[11] Chang and colleagues[11] concluded that Narp contributes to the antidepressant action of ECT and that ECS can induce dendritic arborization.

ECT has been shown to induce hippocampal neurogenesis[12] and neuroplasticity.[13] Schloesser and colleagues[14] reported that ECS leads to antidepressant effects with concurrent hippocampal neurogenesis. Neuroimaging studies[15] have revealed that ECT induces neuroplastic processes in the amygdala and hippocampus that are associated with improved clinical response in MDD. Although a complete understanding of